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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,826	12/19/2001	Hans-Georg Ihlenfeldt	BMID9918CUS	4203

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EXAMINER	
FORMAN, BETTY J	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,826	IHLENFELDT ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,16 and 18-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,16 and 18-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 31 March 2004 has been entered.

Status of the Claims

2. This action is in response to papers filed 31 March 2004 in which claims 15, 20, 25 and 26 were amended and claim 17 was canceled. The amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 9 January 2004are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection are discussed.

Claims 15-16 and 18-26 are under prosecution.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The claims are drawn to a composition comprising one or more nucleoside triphosphates (NTP) having a pH of between 8 and 10 and the solution being free of stabilizing substances. The claims further recite, "a PCR function test is positive after about 90 days at a temperature of 35° C." The recited functionality of the composition does not define or describe structural elements or components of the composition. Hence, the functionality does not define the composition over the prior art.

Furthermore, the open claim language "comprising" encompasses any additional elements in prior art compositions.

The courts have stated that a product must be defined over the prior art in terms of it's structure rather than function see *In re Danly*, 263 F.2d 844, 847, 120 USPQ 528, 531 (CCPA1959). "[A]pparatus claims cover what a device is, not what a device does." Hewlett-Packard Co. v. Bausch & Lomb Inc., 909 F.2d 1464, 1469, 15 USPQ2d 1525,1528 (Fed. Cir. 1990) (see MPEP, 2114).

4. Claims 15, 19-21 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Mullis et al (U.S. Patent No. 4,965,188, issued 23 October 1990).

Regarding Claim 15, Mullis discloses an aqueous solution comprising NTPs having a pH value of between 8 and 10 and free of stabilizing substances. Mullis specifically teaches an embodiment comprising an aqueous amplification mixture comprising NTPs wherein the pH is 8 (Column 10, lines 40-44; Column 29, lines 10-16 and Column 34, lines 34-40).

Regarding Claim 19, Mullis discloses the NTPs are deoxy NTP (Column 29, lines 10-16).

Regarding Claim 20, Mullis discloses the composition comprising a substance which buffers between 8 and 10 i.e. Tris HCL (Column 29, lines 10-16).

Regarding Claim 21, Mullis discloses a method for replicating via reverse transcriptase using the composition of Claim 15 (Column 34, lines 34-40).

Regarding Claim 25, Mullis discloses a method for synthesizing nucleic acids using the composition comprising NTPs having a pH value of between 8 and 10 and free of stabilizing substances. Mullis specifically teaches an embodiment comprising an aqueous amplification mixture comprising NTPs wherein the pH is 8 (Column 10, lines 40-44; Column 29, lines 10-16).

5. Claims 15, 19, 20 and 25 are rejected under 35 U.S.C. 102(e) as being anticipated by Persing et al (U.S. Patent No. 5,643,723, filed 26 May 1994).

Regarding Claim 15, Persing discloses an aqueous solution comprising NTPs having a pH value of between 8 and 10 and free of stabilizing substances. Persing specifically teaches

an embodiment comprising an aqueous amplification "Master Mix" comprising NTPs wherein the pH is 8.3 (Column 4, lines 40-51 and Column 16, line 54-Column 17, line 15).

Regarding Claim 19, Persing discloses the NTPs are deoxy NTP (Column 4, lines 40-51 and Column 16, line 54-Column 17, line 15).

Regarding Claim 20, Persing discloses the composition comprising a substance which buffers between 8 and 10 i.e. Tris HCL Column 16, line 54-Column 17, line 15).

Regarding Claim 25, Persing discloses a method for synthesizing nucleic acids using the composition comprising NTPs having a pH value of between 8 and 10 and free of stabilizing substances. Persing specifically teaches an embodiment comprising an aqueous amplification mixture comprising NTPs wherein the pH is 8.3 (Column 4, lines 40-51 and Column 16, line 54-Column 17, line 15).

6. Claims 15, 19, 20 and 25 are rejected under 35 U.S.C. 102(e) as being anticipated by Nishimura et al (U.S. Patent No. 5,935,825, filed 18 November 1994).

Regarding Claim 15, Nishimura discloses an aqueous solution comprising NTPs having a pH value of between 8 and 10 and free of stabilizing substances. Nishimura specifically teaches an embodiment comprising an aqueous amplification mixture comprising NTPs wherein the pH is 8.3-10 (Column 4, lines 40-60).

Regarding Claim 19, Nishimura discloses the NTPs are deoxy NTP (Column 4, lines 54-58).

Regarding Claim 20, Nishimura discloses the composition comprising a substance which buffers between 8 and 10 i.e. Tris HCL (Column 4, lines 40-50).

Regarding Claim 25, Nishimura discloses a method for synthesizing nucleic acids using an aqueous solution comprising NTPs having a pH value of between 8 and 10 and free of stabilizing substances. Nishimura specifically teaches an embodiment comprising an aqueous amplification mixture comprising NTPs wherein the pH is 8.3-10 (Column 4, lines 40-60).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mullis et al (U.S. Patent No. 4,965,188, issued 23 October 1990) in view of Promega catalog (1992-1993, page 170).

Regarding Claim 18, Mullis discloses an aqueous solution comprising NTPs having a pH value of between 8 and 10 and free of stabilizing substances. Mullis specifically teaches an embodiment comprising an aqueous amplification mixture comprising NTPs wherein the pH is 8 (Column 10, lines 40-44; Column 29, lines 10-16 and Column 34, lines 34-40). Mullis teaches the composition wherein the concentration of the NTPs is 1.5m M. While Mullis does not teach the claimed 2-200m M concentration, the claimed concentration was well known in

the art at the time the claimed invention was made as taught by Promega (see web site description). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to slightly increase the NTP concentration of Mullis to the claimed concentration because one of ordinary skill in the art would have expected the concentrations to have similar properties. One of ordinary skill would have been motivated to adjust the NTP concentration using routine experimentation to derive the optimal concentration for the expected benefit of optimizing composition performance.

It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

The courts have stated where the claimed ranges "overlap or lie inside the ranges disclose by the prior art" and even when the claimed ranges and prior art ranges do not overlap but are closed enough that one skilled in the art would have expected them to have similar properties, a *prima facie* case of obviousness exists (see *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775. 227 USPQ 773 (Fed. Cir. 1985) (see MPEP, 2144.05 I.).

Therefore, the claimed ranges would have been obvious in view of the teaching of Mullis.

9. Claims 16 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mullis et al (U.S. Patent No. 4,965,188, issued 23 October 1990) in view of Gibco BRL catalog (1993, page 300).

Regarding Claims 16 and 26, Mullis discloses an aqueous solution comprising NTPs having a pH value of between 8 and 10 and free of stabilizing substances. Mullis specifically teaches an embodiment comprising an aqueous amplification mixture comprising NTPs wherein the pH is 8 (Column 10, lines 40-44; Column 29, lines 10-16 and Column 34, lines 34-40). Mullis does not teach modified NTPs or dideoxynucleotide triphosphates (ddNTP).

However, modified nucleoside triphosphates (ddNTPs) in aqueous solutions were well known in the art at the time the claimed invention was made as taught by Gibco BRL. Specifically, Gibco BRL teaches a similar aqueous nucleoside triphosphate solution free from stabilizers wherein the nucleoside triphosphates are modified i.e. ddATP (page 300, Catalog No. 8243C). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify nucleoside triphosphate of Mullis with the modified nucleoside triphosphates taught by Gibco BRL for the expected benefit of providing detectable nucleosides based on the modification e.g. termination of extension product.

10. Claims 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mullis et al (U.S. Patent No. 4,965,188, issued 23 October 1990), in view of Sambrook ("Molecular Cloning: a laboratory manual", 1992, 10.6-10.17 and 13.3-13.6)

The claims are drawn methods for sequencing nucleic acid sequences (Claim 22), random priming of nucleic acid sequences (Claim 23) and nick translation of nucleic acid

sequences (Claim 24). The claimed methods are acknowledged by applicant as known in the art wherein the improvement being the methods comprising the solution according to Claim 15.

Regarding Claims 22-24, Mullis discloses an aqueous solution comprising NTPs having a pH value of between 8 and 10 and free of stabilizing substances. Mullis specifically teaches an embodiment comprising an aqueous amplification mixture comprising NTPs wherein the pH is 8 (Column 10, lines 40-44; Column 29, lines 10-16 and Column 34, lines 34-40). Mullis teaches use of the compositions but they do not specifically teach sequencing, random priming or nick translation. However, use of NTP compositions in these methods was well known in the art at the time the claimed invention was made as taught by Sambrook (10.6-10.17 and 13.3-13.6).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to utilize the NTP composition of Mullis in the instantly claimed methods because one of ordinary skill in the art would have expected the NTP composition to function in sequencing, random priming and nick translation based on the teaching of Sambrook.

11. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nishimura et al (U.S. Patent No. 5,935,825, filed 18 November 1994) in view of Promega catalog (1992-1993, page 170).

Regarding Claim 18, Nishimura discloses an aqueous solution comprising NTPs having a pH value of between 8 and 10 and free of stabilizing substances. Nishimura specifically

teaches an embodiment comprising an aqueous amplification mixture comprising NTPs wherein the pH is 8.3-10 (Column 4, lines 40-60) but does not teach the claimed 2-200m M concentration. However, the claimed concentration was well known in the art at the time the claimed invention was made as taught by Promega (see web site description). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to slightly increase the NTP concentration of Nishimura to the claimed concentration because one of ordinary skill in the art would have expected the concentrations to have similar properties. One of ordinary skill would have been motivated to adjust the NTP concentration using routine experimentation to derive the optimal concentration for the expected benefit of optimizing composition performance.

12. Claims 16 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nishimura et al (U.S. Patent No. 5,935,825, filed 18 November 1994) in view of Gibco BRL catalog (1993, page 300).

Regarding Claims 16 and 26, Nishimura discloses an aqueous solution comprising NTPs having a pH value of between 8 and 10 and free of stabilizing substances. Nishimura specifically teaches an embodiment comprising an aqueous amplification mixture comprising NTPs wherein the pH is 8.3-10 (Column 4, lines 40-60) but does not teach modified NTPs or dideoxynucleotide triphosphates (ddNTP).

However, modified nucleoside triphosphates (ddNTPs) in aqueous solutions were well known in the art at the time the claimed invention was made as taught by Gibco BRL.

Specifically, Gibco BRL teaches a similar aqueous nucleoside triphosphate solution free from stabilizers wherein the nucleoside triphosphates are modified i.e. ddATP (page 300, Catalog No. 8243C). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify nucleoside triphosphate of Nishimura with the modified nucleoside triphosphates taught by Gibco BRL for the expected benefit of providing detectable nucleosides based on the modification e.g. termination of extension product.

13. Claims 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nishimura et al (U.S. Patent No. 5,935,825, filed 18 November 1994) in view of Sambrook ("Molecular Cloning: a laboratory manual", 1992, 10.6-10.17 and 13.3-13.6)

The claims are drawn methods for reverse transcription (Claim 21), sequencing nucleic acid sequences (Claim 22), random priming of nucleic acid sequences (Claim 23) and nick translation of nucleic acid sequences (Claim 24). The claimed methods are acknowledged by applicant as known in the art wherein the improvement being the methods comprising the solution according to Claim 15.

Regarding Claims 21-24, Nishimura discloses an aqueous solution comprising NTPs having a pH value of between 8 and 10 and free of stabilizing substances. Nishimura specifically teaches an embodiment comprising an aqueous amplification mixture comprising NTPs wherein the pH is 8.3-10 (Column 4, lines 40-60) and teaches use of the compositions but they do not specifically teach reverse transcription, sequencing, random priming or nick translation. However, use of NTP compositions in these methods was well known in the art at the time the claimed invention was made as taught by Sambrook (10.6-10.17 and 13.3-13.6).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to utilize the NTP composition of Nishimura in the instantly claimed methods because one of ordinary skill in the art would have expected the NTP composition to function in sequencing, random priming and nick translation based on the teaching of Sambrook.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
June 7, 2004